The Causes of Absorption of Oxygen by the Lungs (Preliminary Communication).

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It has for long been a subject of controversy among physiologists whether the absorption of oxygen through the walls of the lung alveoli into the blood occurs simply by diffusion or by an active physiological process analogous to glandular secretion.* Pflüger, Fredericq, and, quite recently, Krogh,† have brought forward experimental evidence in favour of the diffusion theory, while Bohr, and Haldane and Lorrain Smith have supported the secretory theory, which was originally suggested by Ludwig.

If the partial pressure of oxygen is ever greater in the arterial blood leaving the lungs than in the air of the lung alveoli, it is clear that the simple diffusion theory must fall to the ground; and the experiments hitherto made have been designed to ascertain whether or not the oxygen pressure in the arterial blood is ever greater than in the alveolar air. Bohr, Fredericq, and Krogh have with this object employed improved forms of Pflüger's well-known "aerotonometer," the instrument finally devised by Krogh being very perfect of its kind. Haldane and Lorrain Smith's method depends upon the following facts:—When blood is brought into prolonged and intimate contact with a mixture of carbon monoxide and air the hæmoglobin of the blood-corpuscles combines partly with the oxygen and partly with the carbon monoxide, the final proportions (which can be easily and accurately determined) depending, in accordance with the laws of mass-action, on the relative partial pressures of the oxygen and carbon monoxide, and on a constant. Hence, if the final proportions, the constant, and the partial pressure of the carbon monoxide are known, the partial pressure of the oxygen can be accurately deduced. By supplying to an animal air containing a fixed proportion of carbon monoxide, until the final saturation of its hæmoglobin with carbon monoxide is reached, the partial pressure of oxygen in its arterial blood can be calculated on the same principle. If the arterial oxygen pressure is greater than that of the alveolar air the final saturation of the hæmoglobin with carbon monoxide will be less than that of blood saturated

* A comprehensive account of this controversy is given by Bohr in Nagel's 'Handbuch der Physiologie,' vol. 1, p. 142, 1905.

† 'Skand. Archiv für Physiologie,' vol. 23, pp. 179—278, 1910.

with the same air outside the body, and *vice versâ*. It is, of course, assumed that carbon monoxide diffuses freely through the body, since, apart from its property of combining with the hæmoglobin, it is, as was experimentally shown by Haldane, a physiologically indifferent gas, like nitrogen or hydrogen.

Haldane and Lorrain Smith determined the constants required in their calculations, not from experiments at body temperature on blood from the animals experimented on, but on dilute blood solutions or undiluted human blood. This omission, which in the then existing state of knowledge did not seem important, has, we find, seriously affected their estimates of the oxygen pressure in the arterial blood. The constant varies distinctly for the blood of different animals, and even for different individuals of the same species. We have, therefore, repeated the experiments, using mice, on which most of Haldane and Lorrain Smith's experiments were made, and determining the constant for the blood of each animal experimented on. We find that in general their estimates of oxygen tension were about a third too high.

We have also supplied an omission in their experiments by investigating the arterial oxygen pressure in animals breathing a very low percentage of carbon monoxide (less than 0·02 per cent.), so that no physiological disturbance is produced by the gas.

Our results with mice are as follows:—

1. When a very low percentage of carbon-monoxide is breathed, so that no want of oxygen is produced in the body, the arterial oxygen pressure is slightly *below* the alveolar oxygen pressure. Apparently, therefore, the absorption of oxygen is by diffusion alone, as indicated by the experiments of Fredericq and Krogh, and by most of Bohr's experiments. The results agree closely with Bohr's recent calculations of the arterial oxygen pressure which might be expected during rest if diffusion alone were in play.

2. When a much higher percentage of CO is breathed (0·2 per cent. or more) the oxygen pressure in the arterial blood rises to nearly double that of the alveolar air, and considerably above that of the external air. With intermediate percentages of CO there are intermediate rises in the arterial oxygen pressure.

It is thus evident that, although under normal resting conditions absorption of oxygen occurs only by diffusion, want of oxygen in the tissues of the body brings into play a supplementary secretory activity by which oxygen is *actively* absorbed from the alveolar air into the blood. This process is presumably analogous to that by which oxygen at a partial pressure of sometimes as much as 100 atmospheres above that in the sea water is secreted into the swim-bladder of deep-sea fishes.

It is satisfactory to find that the results by the carbon-monoxide method agree closely with those hitherto obtained by the aerotonometer method. The reasons why Fredericq and Krogh have obtained no evidence in favour of the secretion theory are also evident. Still more satisfactory is it to find that the process of absorption of oxygen by the lungs is regulated, just as is the breathing itself, in accordance with the physiological requirements of the organism. But for the secretory process the blood would be very incompletely saturated during muscular work, when five, or even ten, times as much oxygen is absorbed as during rest. During rest, on the other hand, the secretory process is not required, and would be a waste of physiological effort.

The Action of Nicotine and other Pyridine Bases upon Muscle.

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Nicotine, or pyridyl *n*-methyl pyrrolidine, $C_5H_4N.C_4H_7N(CH_3)$ (m.w. = 162), best known to physiologists in this country in connection with its action on sympathetic ganglia as pointed out by Langley, is generally regarded as having little or no action upon muscle.

According to recent observations of Langley the drug does, however, act upon muscle in a peculiar way, that has led him to a theoretical interpretation which we shall consider later. Our original purpose was the simpler one of comparing upon muscle the action of nicotine and allied substances.

We have made, independently, two separate series of observations, one during September, 1908, with nicotine tartrate, $C_{10}H_{14}N_2.2C_4H_6O_6.2H_2O = 498$, the other during September, 1909, with the free base, following the method described in previous communications, according to which the muscle is excited at intervals throughout observation.

In both series, with differences of detail attributable to the fact that the tartrate in solution is probably to some extent hydrolysed, the nicotine record is unmistakably characteristic, and not presented by any other substance that we have examined. Both in the case of the salt and in that of the base, the drug in moderate concentration produced :—

(1) Contracture with twitching.

(2) A first diminution of contraction not reaching to complete abolition.